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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/971,813	10/05/2001	Nicholas W. Warne	22058-531CON (GI-5371)	3576

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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/971,813	WARNE ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/06/02, 2/25/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

3. For convenience, claim 1 is reproduced below.

1. **(currently amended) A composition comprising IL-11, glycine and a cryoprotectant, wherein said IL-11 in said composition shows reduced aggregation following storage for 26 weeks at 40° C as compared to IL-11 stored for 26 weeks at 40° C in a composition with glycine and without said cryoprotectant.**

4. As presently worded, the composition may comprise virtually any one or combinations of "IL-11" as the product is not defined in terms of any activity, source, amino acid composition, etc. Indeed, the specification teaches at page 7, lines 23-25, teach:

> As is appreciated by one skilled in the art, any form of IL-11 which retains IL-11 activity, such as variants through the substitution or deletion of amino acids, analogs and derivatives of IL-11, is useful according to the present invention...
>
> In addition to recombinant techniques, IL-11 may also be produced by known conventional chemical synthesis. Methods for constructing the polypeptides useful in the present invention by synthetic means are known to those of skill in the art. The synthetically constructed cytokine polypeptide sequences, by virtue of sharing primary, secondary, or tertiary structural and conformational characteristics with the natural cytokine polypeptides are anticipated to possess biological activities in common therewith. Such synthetically constructed cytokine polypeptide sequences or fragments thereof, which duplicate or partially duplicate the functionality thereof may also be used in the compositions of this invention. Thus, they may be employed as biologically active or immunological substituents for the natural, purified cytokines useful in the present invention.

A review of the disclosure fails to find any amino acid sequence for any version of IL-11 has been provided. Furthermore, the disclosure fails to teach which structures/conformations and amino acid residues are required for any level of activity, much less a detailed teaching of where and to what degree the base sequence of IL-11 as found in any life form can be substituted, deleted, or otherwise derived. Given that the claims fairly encompass just such embodiments, and the specification does not provide an adequate written description of same, the specification does not reasonably suggest that applicant was in possession of the claimed invention at the time of filing.

5. As presently worded, the claimed composition fairly encompasses having a cryoprotectants present at virtually any concentration, and that the composition can be at virtually any pH, and activity, or no activity. A review of the disclosure, however, finds support for cryoprotectants being present at a range of from about 0.5% to about 5%, and that when the cryoprotectants is sucrose, that it be present at a rage of from about 0.5% to about 2%; see page 3, second full paragraph. Said page 3 has also been found to provide support for a range in pH of from about 6.0 to about 8.0; that the buffering agent be present at a concentration of from about 1 mM to about 100 mM; and that a bulking agent, e.g., glycine, is present at a concentration of about 1 mM to about 1 M. A review of the disclosure fails to find adequate support, which reasonably suggests that applicant had contemplated, much less reasonably suggests possession of, alternative formulations. In view of the limited disclosure, applicant is urged to narrow the claims' scope such they more closely parallel the support found in the disclosure.

6. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

New Matter

The amendment to claim 1 has introduced new matter into said claim. Acknowledgement is made of applicant's representative directing attention to various passages of the specification as providing support for the newly added limitations. Said passages have been reviewed and have not been found to support the breadth of scope provided. It is noted that the results recited in the claim were that produced under a specific set of conditions. Claim 1 is not so limited and a review of the disclosure fails to find where a broader set of conditions were contemplated and

which were to result in the same observation. Accordingly, and in the absence of convincing evidence to the contrary, claim 1, and claims 2-25 that depend therefrom, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 6, 9, 10, 21, 22, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of said claims recites that a component of a composition is to be present in a percentage (%), however, the basis or relationship upon which one is to calculate the percentage is not recited. Consequently, one is not able to readily determine the metes and bounds of the claims.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,371,193 (Bennett et al.), US Patent 5,679,339 (Keith et al.), and US Patent 6,096,873 (Schaefer et al.).

13. Bennett et al., disclose and claim (claim 4) a pharmaceutical composition comprising IL-II. Column 9 states in part "[t]he preparation of such a pharmaceutically acceptable protein solution, having due regard to pH, isotonicity, stability and the like, is within the skill of the art.

14. Bennett does not set forth in specific detail the concentrations and additives specifically identified in the now claimed composition.

15. Keith et al., at columns 7 and 8, disclose various compositions of IL-II. As seen therein, the compositions may comprise polyethylene glycol, single amino acids such as glycine or histidine, sucrose, and various concentrations. At column 8, fifth paragraph, the preparation of a lyophilized composition of IL-II is disclosed; a limitation of claim 25.

16. Keith et al., do not disclose the inclusion of methionine or TWEEN 20 in the composition.

17. Schaefer et al., disclose a multitude of commonly accepted pharmaceutical formulations. While the disclosure is directed to gamma-heregulin, a polypeptide that stimulates the growth of cells, such disclosure is directly applicable to the formulations of IL-II as both heregulin and IL-II are proteins that act upon cells. At column 27, last paragraph, bridging to column 28, first paragraph, there is disclosed the concept of including in a pharmaceutical composition low molecular weight proteins that are further characterized as having less than 10 amino acids. Such renders obvious the inclusion of the antioxidant L-methionine (a limitation of claims 11-14, 23, and 24) as well as glycine (a limitation of claims 1-25). In column 28, the inclusion of disaccharides renders obvious the inclusion of the cryoprotectant sucrose; a limitation of claims 1-25. The inclusion of surfactants generally, renders obvious the inclusion of polysorbate, a limitation of claims 7-10, 22, and 23. Schaefer et al., also teach specifically of including any of the surfactants sold under the trademark of TWEEN (polysorbates; column 28); this meets a limitation of claim 8.

18. In view of the totality of the teachings in the art as to the preparation of any number of formulations of polypeptide-containing compositions which act upon a cellular process, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have expanded upon the "pharmaceutical composition" taught by Bennett et al., so to include the added reagents and formulations disclosed by both Keith et al., and Schaefer et al.

19. In view of the profound medical significance imparted to IL-II, the ordinary artisan would have been highly motivated to prepare such pharmaceutical compositions and in view of

the well-developed nature of this part of the pharmaceutical art, said ordinary artisan would have had a reasonable expectation of success. For the above reasons and in the absence of convincing evidence to the contrary, the claimed invention is considered to be obvious in view of the prior art of record.

Response to argument

20. At page 7 of the response received 25 February 2005, hereinafter the response, applicant's representative asserts "there is no suggestion in the Bennett, Keith, or Schaefer [references] that combining IL-11 with glycine and a cryoprotectants would result in any added benefit, much less result in a composition characterized by reduced aggregation following prolonged storage, as required by the claims. Nor is there a reasonable expectation of success in making a composition with the required properties."

21. The above argument has been fully considered and has not been found persuasive. At page 6 of the disclosure applicant states:

22. "[T]he addition of a bulking agent such as glycine, a cryoprotectant such as sucrose and/or polysorbate such as TWEEN-20® acts to prevent aggregation of IL-11 and protects IL-11 from the harmful effects of shearing and freezing."

23. It is well settled that a compound and its properties are inseparable. As shown above, applicant has recognized that certain properties are observed when a composition comprising IL-11 and a bulking agent and a cryoprotectant are combined. Accordingly, the question is whether one of skill in the art at the time the instant application was filed would have been motivated to combine these same components. As shown above, the art fairly teaches the combining of IL-11 along with just such a bulking agent (glycine) and a cryoprotectant (sucrose as well as

polysorbate). While the art may well be silent as to its recognition of this specific property, the identification of a new property does not make an old composition now patentable. Clearly, the prior art teaches formulating IL-11 in any of a variety of manners, and the present formulation is arguably an optimization of such. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

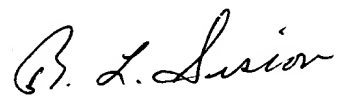
24. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,371,193 (Bennett et al.), US Patent 5,679,339 (Keith et al.), and US Patent 6,096,873 (Schaefer et al.).

Conclusion

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

26. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

27. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
18 May 2005